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I, JULIE BILLINGSLEY, TEAM LEADER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. PS 0016 for a patent by SGE INTERNATIONAL PTY LTD as filed on 17 January 2002.

WITNESS my hand this
Thirteenth day of July 2004

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PROVISIONAL SPECIFICATION

Invention Title: **Chromatography column**

The invention is described in the following statement:

CHROMATOGRAPHY COLUMN

Field of the Invention

The present invention relates to liquid chromatography and in particular to capillary and micro liquid chromatography columns.

Background of the Invention

Liquid chromatography is used for separation of certain compounds by their interaction with a packed bed in a separation column. The molecules to be separated are dissolved in a liquid mobile phase that is pumped through the packed bed, which is packed tightly, usually into a tube.

A liquid chromatography system typically comprises a pump to generate the flow and high pressure necessary to force the liquid mobile phase through the separation column. An injection valve then introduces a measured amount of the sample to be analysed into the liquid mobile phase stream. There may be a pre-column or in-line filter after the injection valve to remove particulate matter or material from the liquid mobile phase that may damage the separation column. The liquid mobile phase is pumped through the separation column under high pressure and the effluent of the separation column is carried to a detection system that is used to measure and quantitate the separated sample components.

Between each of the components in the liquid chromatography system there are typically connections made to transfer lines to take the liquid flow from one component of the system to the next. The flowpath of the liquid therefore includes several joints which must be sealed against high pressure without introducing detrimental effects to the flowpath.

Within a conventional separation column design there are connections from the connecting tubing, to the column endfitting (usually containing a frit), between the endfitting and the separation column itself, and then the same is repeated on the other end of the separation column. The frit devices are required to keep the particulate separation media contained within the separation column.

Existing separation columns were designed when liquid chromatography columns were large, greater than 2.0mm inside diameter, for example. The relatively large flowrates meant that components were less critical to join without introducing deleterious affects to the performance of the system. Microbore (typically between 1.0mm - 2.1mm internal diameter) and capillary bore (typically less than 1.0mm internal diameter) liquid chromatography systems are becoming more commonplace and a better approach is needed to obtain good performance of the liquid chromatography system and to ensure that the making of connections for the less skilled practitioner is less critical.

It is therefore an object of this invention to provide a liquid chromatography system incorporating low volume and zero dead volume connections.

Summary of the Invention

The invention accordingly provides a liquid chromatography system including:

a separation column having an internal bore;

an end fitting assembly fitted at one side to an end of the separation column; and

transfer tubing fitted to the opposite side of the end fitting;

wherein the separation column, transfer tubing, and end fitting assembly are constructed as a sealed integral system.

Preferably, the separation column is a micro or capillary liquid chromatography column. More preferably, the internal diameter of the internal bore of the separation column is in the range 0.030mm – 1.0mm.

The end fitting assembly advantageously includes a backing ferrule and a double ferrule incorporating a frit.

The double ferrule preferably includes central bore which aligns with the bore of the separation column and the bore of the transfer tubing when the system is assembled. The double ferrule is preferably formed as a double-conical shaped component, tapering from the middle of the ferrule to either end of the ferrule.

The frit of the double ferrule may be a wire mesh frit or a polymer or metal frit formed in the ferrule.

The liquid chromatography system preferably further includes a protective outer tubular sheath surrounding the separation column, and preferably extending over at least part of the double ferrule. The sheath may be made of metal and serves to give strength to the system and prevent the small outside diameter separation column from being damaged in use.

Advantageously, the backing ferrule is received within the protective sheath surrounding the separation column. The backing ferrule includes a central bore sized to receive the separation column therethrough, and the outer diameter of the backing ferrule is sized to be received within the protective sheath surrounding the separation column. The end of the backing ferrule received within the sheath is preferably generally perpendicular to the axis of the separation column. The opposite end of the backing ferrule is a hollow conical shape to receive one side of the double ferrule and to form the ferrule into a permanent seal onto the separation column. The separation column preferably extends through the backing ferrule and into the double ferrule. Preferably the separation column extends midway along the bore of the double ferrule up to one side of the frit.

Preferably the separation column is made of glass lined metal tubing or fused silica lined polymer tubing.

A transfer or connecting tubing is provided on the other side of the double ferrule. Advantageously, the transfer tubing is received within the bore of the double ferrule and also extends midway along the length of the double ferrule up to the side of the frit opposite the separation column. The bore of the double

ferrule may be stepped to accommodate a separation column and transfer tubing of different outer diameters.

Advantageously, the double ferrule is permanently collapsed so as to fix the capillary column into one end and the transfer tubing into its other end.

Brief Description of the Drawing

The invention will now be described by way of example, with reference to the accompanying drawing which is a side cross-sectional view of an integral liquid chromatography column according to an embodiment of the invention.

Description of Preferred Embodiments

Referring to the drawing there is illustrated a liquid chromatography system 10 according to an embodiment of the invention. The system 10 includes separation column 12, outer protective sheath 14, backing ferrule 16, double ferrule 18 incorporating frit 20, and transfer or connecting tubing 22 to other devices such as the sample introduction valve and detector (not shown). The backing ferrule 16, double ferrule 18, frit 20, and transfer tubing 22 are repeated at the opposite end (not shown) of the separation column 12.

Separation column 12 is preferably either a micro or capillary liquid chromatography column. The separation column 12 is preferably made of glass lined metal tubing or fused silica lined polymer tubing. The internal bore 13 of the column 12 is tightly packed with packing material (not shown). The separation column 12 is contained within protective sheath 14 that extends along the length of the column 12 and covers at least part of the double ferrule 18 as discussed below. Sheath 14 is advantageously made of a polymer or metal and serves to reduce accidental damage to the separation column 12.

Backing ferrule 16 is provided at each end of the separation column 12 (only one end is illustrated). Backing ferrule 16 includes a central bore 17 sized to receive the separation column 12. The outer diameter of the backing ferrule is sized to be closely received within the outer sheath 14. The side 19 of the backing

ferrule 16 facing the separation column 12 is generally perpendicular to the axis of the separation column, while the other side 21 of the backing ferrule is shaped as a hollow cone 23, as illustrated, to receive one side 24 of the double ferrule 18 and to form the ferrule 18 into a permanent seal onto the separation column 12.

Double ferrule 18 is formed as a double-sided conical component, tapering from the middle of the component to each side 24, 25. The double ferrule also includes a central bore 26 extending therethrough. A first side 24 of the double ferrule is tightly received within the hollow conical portion 23 of backing ferrule 16. Sheath 14 advantageously extends up to midway along the double ferrule.

The frit 20 is captured in the double ferrule 18 either as a wire mesh frit or a polymer or metal frit formed in the ferrule 18. Frit 20 is a flat circular disc with a plurality of holes that acts as a filter of the packing material. The frit 20 is preferably located in or near the middle of the double ferrule 18. The separation column preferably extends through the backing ferrule 16, and into the double ferrule 18 up to the frit 20.

The second side 25 of the double ferrule extends from the cover of the sheath 14 and receives one end of transfer or connecting tubing 22. The transfer tubing preferably extends into the double ferrule 18 up to side of the frit opposite the separation column 12.

Advantageously, the double ferrule 18 is permanently collapsed so as to fix the separation column 12 into one end 24 and the transfer tubing 22 into its other end 25.

Ideally the tubing of the separation column 12 and transfer tubing 22 should have an outside diameter as small as possible. A small outside diameter reduces the annular area at connections proportional to the square of the diameter, which helps reduce unwanted dead volumes within the system.

The ferrule 18 is designed and is of small enough dimension to permit machining to the very precise dimensions and concentricity required in the join

between the separation column.12 and transfer tubing 22. The bore of the double ferrule may be stepped to accommodate a separation column and transfer tubing of different outer diameters.

The integrated liquid chromatography column can be produced using various diameter components and materials, for example, 1/16" outer diameter (OD) glass lined metal tubing (GLT), 0.635mm O.D. GLT, 1/16" OD PEEKSIL and 1/32" OD PEEKSIL for the column tubing material. PEEKSIL is a fused silica capillary tube coated with PEEK (polyetheretherketone). The inside diameter of the separation column is typically between 0.030mm and 1.0mm.

The transfer tubing 22 is preferably either 1/16" OD or 1/32" OD fused silica lined PEEK which has an inside diameter of between 0.010mm and 0.100mm. Another suitable connecting tubing material is fused silica tubing with 0.010mm to 0.100mm inside diameter range and an outer protective coating of polyamide to give approximately 0.35mm OD.

It will be appreciated that the chromatography column of the invention is designed to incorporate all critical elements of the column into a permanently sealed fitting. In this way the column can be designed to achieve ideal flowpath properties because there is no need to make the system in several pieces as is the usual practice in liquid chromatography fittings. Typical error build-ups in assembly of the system is therefore not an issue. It will also be appreciated that the double ferrule of the system is an easy component to machine in very high volume and is therefore a much less expensive way to produce a liquid chromatography column.

It will be understood that the invention disclosed and defined in this specification extends to all alternative combinations of two or more of the individual features mentioned or evident from the text or drawings. All of these different combinations constitute various alternative aspects of the invention.

SGE International Pty Ltd
By its Registered Patent Attorneys
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17 January 2002

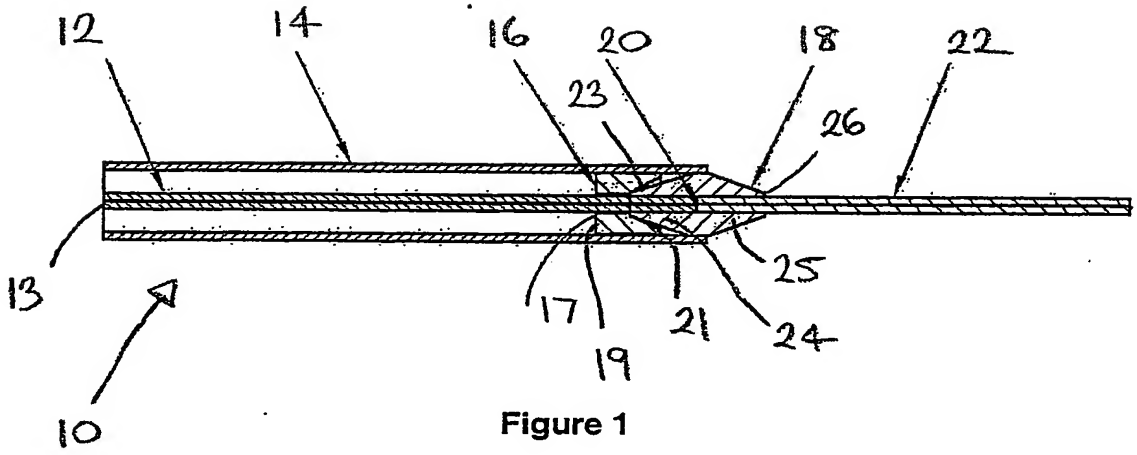

Figure 1